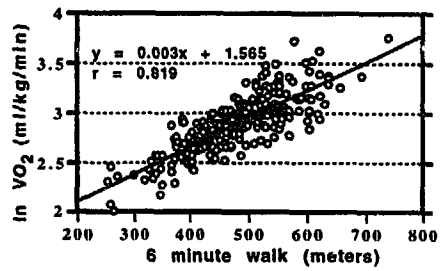
analysis. Linear regression models were developed to predict ln(VO_2max) from 6MW with and without BSA, age, and sex.



Inclusion of BSA and age significantly improved the model (ln[VO_2max] *in ml/min* = 4.569 + 0.0026 (6MW) + 0.838 BSA – 0.0036 Age; r = 0.902). In conclusion, use of this regression model may, if validated, allow accurate prediction of VO_2 max from 6MW.

952-115 Arachidonic Acid-Induced Dilation of Epicardial Coronary Artery Is Maintained in Awake Dogs With Chronic Exercise Training Plus Rapid Cardiac Pacing

Geng-Hua Yi, Daniel Burkhoff, Mathias Knecht, Sulli Popilskis, Milton Packer, Jie Wang. *Columbia Univ. College of P&S, New York, NY*

Previous studies has shown that arachidonic acid(AA)-induced dilation of epicardial coronary artery (CA) is attenuated but PGI_2-induced dilation of CA is preserved in heart failure (CHF), suggesting that the attenuated response of AA is due to defective endothelial conversion of AA to prostacyclins. Since exercise training (EX) normalizes some aspects of endothelial function, the objective of this study was to determine whether EX improves AA-induced dilation of CA during development of CHF. Dogs(n = 6) were chronically instrumented for measurements of left ventricular and aortic pressure, coronary blood flow and diameter of CA and for chronic cardiac pacing. Dogs were cardiac paced for 4 wks and treadmill EX (4.4 ± 0.36 km/hour) was performed on a treadmill 2 hours/day throughout this 4 wks. Changes in CA diameter induced by AA were examined before (*Control*) and after this 4 wk period (*Pacing plus exercise*). The results are as follows:

	Baseline	Response	Δ	% Δ
Control				
AA 250 μg/kg	3.50 ± 0.26	3.63 ± 0.25	0.14 ± 0.03*	4.15 ± 1.10*
AA 500 μg/kg	3.50 ± 0.26	3.68 ± 0.26	0.18 ± 0.05*	5.23 ± 1.57*
After 4 wk pacing plus exercise				
AA 250 μg/kg	3.81 ± 0.21	3.93 ± 0.20	0.13 ± 0.02*	3.47 ± 0.74*
AA 500 μg/kg	3.79 ± 0.22	3.96 ± 0.22	0.17 ± 0.02*	4.52 ± 0.76*

values are CA diameter in mm. *p < 0.05 from baseline

This contrasts with previous results showing that the response of CA diameter to AA is eliminated in dogs with the same pacing regimen but without exercise. Thus, EX training protected endothelium/prostaglandin-mediated dilation of CA during development of CHF. This may indicate that the conversion of AA to prostacyclins was normalized by EX.

953 Basic Coronary Vascular Physiology – Miscellaneous

Tuesday, March 26, 1996, 9:00 a.m.–11:00 a.m.
Orange County Convention Center, Hall E
Presentation Hour: 9:00 a.m.–10:00 a.m.

953-89 Natriuretic Peptides Inhibit Endothelin-1 and Angiotensin-II Mediated Human Coronary Smooth Muscle Cell Proliferation

Chi-Ming Wei, John C. Burnett, Jr.. *Mayo Clinic, Rochester, MN*

Atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP) are a family of structurally related peptides that participate in the integrated control of renal and cardiovascular function via activation of particulate guanylyl cyclase and generation of cGMP. While an antimitogenic action for the natriuretic peptides have been investigated in non-human mammalian cells, the antiproliferative action of the natriuretic peptides in human coronary vascular smooth muscle cells (HCVSMC) proliferation remain undefined. Therefore, the current study was designed to investigate the inhibitory function of ANP, BNP and CNP upon endothelin-1 (ET-1) and angiotensin II (AII) mediated HCVSMC proliferation. Cultured HCSMC were stimulated by ET-1 (10^{-7} M) and AII (10^{-7} M) with and without ANP,.BNP and CNP (10^{-7} M each) and thymidine incorporation determined. These studies were repeated with HS-142-1 (10^{-5} M), an antagonist of the natriuretic peptide guanylyl cyclase linked receptors. (cpm/well)

	Control	ET-1	ET-1 + HS	AII	AII + HS
Baseline	190 ± 24	1362 ± 288§		929 ± 186§	
ANP		420 ± 133*	630 ± 278†	161 ± 33*	882 ± 251†
BNP		240 ± 61*	766 ± 223†	156 ± 26*	813 ± 238†
CNP		296 ± 51*	1233 ± 589†	153 ± 30*	592 ± 200†

§p < 0.05 vs control; *p < 0.05 vs baseline; †p < 0.05 vs ET and AII.

These data suggest: (1) ET-1 and AII are potent stimulators for human coronary vascular smooth muscle cells proliferation. (2) ANP, BNP and CNP are potent inhibitors for ET and AII mediated human coronary smooth muscle cell proliferation. (3) These inhibitory actions of ANP, BNP and CNP are mediated by guanylyl cyclase linked natriuretic peptide receptors.

953-90 Interaction of Endothelin-1 With Vasodilators: Effects on Myocardial Contractility and Myocardial Energy Metabolism

Martin E. Beyer, Günther Slesak, Silke Kazmaier, Stefan Nerz, Uwe Helber, Hans Martin Hoffmeister. *Medical Hospital, Dept. III, University of Tübingen, Germany*

In contrast to in vitro experiments, which demonstrated a positive inotropy of endothelin-1 (ET-1), in vivo studies could not detect such a positive inotropy. It was supposed that the direct positive inotropy of ET-1 is counterbalanced in vivo by an indirect cardio-depressant effect due to its vasoconstrictive effect with consequent myocardial ischemia. If this hypothesis is true the positive inotropy of ET-1 should be unmasked by coronary vasodilating drugs.

We examined in open-chest rats whether adenosine (ADO: 2.0 mg/kg/min) or molsidomine (MOL: 5.0 mg/kg) can unmask this positive inotropy of 1.0 nmol/kg ET-1 i. v. by preventing myocardial ischemia. Besides measurements in the intact circulation isovolumic measurements (isovol. LVSP, isovol. dP/dt_{max}) were performed for quantification of myocardial contractility. Additionally myocardial high-energy phosphates were determined (energy charge = [ATP + 1/2ADP]/[ATP + ADP + AMP] as index of ischemia).

	ET-1	ADO + ET-1	MOL + ET-1	NaCl
Isovol. LVSP [%]	104 ± 2	113 ± 2*	108 ± 2*	97 ± 2
Isovol. dP/dt_{max} [%]	98 ± 3	120 ± 3*	115 ± 5*	100 ± 2
TPR [%]	286 ± 21*	236 ± 27*	269 ± 27*	96 ± 3
ATP [μmol/gww]	3.4 ± 0.1*	3.8 ± 0.1	4.3 ± 0.3	4.1 ± 0.1
Energy charge [%]	73 ± 3*	85 ± 2	80 ± 2	84 ± 2

Means ± SEM; hemodynamics in % of preinfusion values, *p < 0.01.

Conclusions: Adenosine and molsidomine antagonize the ET-induced vasoconstriction in part and can unmask the positive inotropy of ET-1 by preventing ET-induced myocardial ischemia.

953-91 Sustained Tissue Nitric Oxide Release After Local Delivery of a Novel Nitric Oxide Donor

David S. Marks, Vincent J. Pompili, Myung H. Jeong, Whyte G. Owen, Zvonimir S. Katusic, David R. Holmes, Jr., Robert S. Schwartz. *Cardiovascular Disease and Special Hematology, Mayo Clinic, Rochester, MN*

Nitric oxide (NO) is a potent vasodilator and platelet inhibitor. The local delivery of small-molecular weight NO-donors has been associated with marked biologic effects extending beyond the short half-life of these compounds. To examine the NO elaborated by vessels exposed to local delivery of NO-donors, we administered a spontaneous NO-donating compound, Dansylpiperazine nonoate (GLO/NO) (1–2 mM) intraluminally to de-endothelialized porcine carotid arteries *ex-vivo*, rinsed the vessel free of the agent, and assayed for nitrite production fluorometrically two hours after local delivery. Nitrite in the supernatant after local delivery of GLO/NO was elevated (771 ± 133 nM/gm tissue) compared to de-endothelialized control (438 ± 68; p = 0.002) and to local delivery of the vehicle (385 ± 34; p = 0.008). GLO/NO treated vessels exhibited marked displaceable NO elaboration after exposure to $HgCl_2$, compared to vehicle (920 ± 148 vs. 370 ± 69; p = 0.001) demonstrating substantial tissue thiol nitrosation by this agent.

Conclusion: Local administration of low molecular weight NO-donors results in marked NO elaboration after treatment. These observations suggest tissue bound NO promotes the prolonged biologic effects after local delivery of NO-donors and suggests a potential therapy to mitigate adverse events after vascular injury.